EFFECT OF INTRATHECAL MAGNESIUM SULPHATE AS AN ADJUNCT TO BUPIVACAINE – FENTANYL IN PATIENTS UNDERGOING ELECTIVE LOWER ABDOMINAL SURGERIES

Dissertation submitted for

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BRANCH X - ANAESTHESIOLOGY

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CERTIFICATE

This is to certify that this dissertation entitled

"Effect of intrathecal magnesium sulphate as an adjunct to bupivacaine fentanyl in patients undergoing elective lower abdominal surgeries – A randomized double blind control study"

is a bonafide record of the work done by Dr.Karthikeyan.S under my supervision and guidance in the department of Anaesthesiology at Thanjavur medical college hospital of Thanjavur Medical College, Thanjavur during the period of his post graduate study from June 2006 to March 2009 for the partial fulfillment of M.D.(Branch X - Anaesthesiology) degree.

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INTRODUCTION

Spinal analgesia was first performed by **August Bier** on 16th august 1898 when he injected 3ml of 0.5% cocaine intrathecally. Spinal anaesthesia is simple, easy to perform and has got a definite endpoint for successful positioning of needle. The spinal analgesia is rapid in onset and the spread of analgesic can be controlled. It requires a small dose of local anaesthetic yet produces profound sensory and motor blockade.

Ever since the introduction of local anaesthetics, diverse classes of drugs such as epinephrine, opioids, clonidine, neostigmine, ketamine and benzodiazepines have been added as adjuvants to local anaesthetics in an attempt to prolong analgesia and reduce the incidence of side effects.

Magnesium has been called "Nature's physiological calcium channel Blocker". Parenteral magnesium has been used for many years on an empirical basis for intraoperative and postoperative analgesia.

Although systemic magnesium decreases postoperative opioid requirements, its intrathecal use has not been evaluated clinically. However, it has been safely used in humans and its safety profile has been documented by histopathological analysis in experimental studies.

In 1906, **Haubold and Meltzer** showed that intrathecal administration of magnesium sulphate produces spinal anaesthesia that includes profound motor and sensory blockade without any permanent untoward effects.

In this prospective randomized double blind controlled study, we evaluated the effect of adding intrathecal magnesium sulphate to bupivacaine and fentanyl in patients undergoing elective lower abdominal surgeries.

AIM OF THE STUDY

To evaluate the effect of intrathecal magnesium sulphate as an adjunct to bupivacaine – fentanyl in patients undergoing elective lower abdominal surgeries.

SPINAL ANAESTHESIA

Spinal (subarachnoid/intrathecal) anaesthesia is a form of central neuraxial block in which a temporary interruption of nerve transmission is achieved following injection of local anesthetic and/or adjuvant solutions into the subarachnoid space. Spinal anaesthesia is the most frequently employed methods of regional anesthesia.

ANATOMY:

The vertebral canal extends from the foramen magnum to the sacral hiatus. It is formed by the dorsal spine, pedicles and lamina of successive vertebrae (7 cervical, 12 thoracic, 5 lumbar and 5 sacral). The vertebrae are held together by a series of overlapping ligaments namely the anterior and posterior longitudinal ligaments, ligamentum flavum, interspinous ligament, supraspinous ligament and the intervertebral discs.

The spinal cord, a direct continuation of the medulla oblongata begins at the upper border of the atlas and terminates distally in the conus medullaris. The distal termination, because of the differential growth rates between the bony vertebral canal and central nervous system varies from L3 in the infant, to the lower border of L1or upper border of L2 in the adult.

Surrounding the spinal cord in the bony vertebral column are three membranes (from within to the periphery), the piamater, arachnoidmater and duramater. The piamater is a highly vascular membrane that closely invests the spinal cord. The arachnoidmater is a delicate neovascular membrane closely attached to the outermost duramater. Between the two innermost membranes is the subarachnoid space. In this space are the cerebrospinal fluid, spinal nerves, blood vessels that supply the spinal cord and the denticulate ligaments. Although the spinal cord ends at the lower border of L1 in adults, the subarachnoid space continues to S2.

The outermost membrane in the spinal canal is the longitudinally organized fibroelastic membrane, the duramater. This layer is the direct extension of the cranial duramater and extends as the spinal duramater from the foramen magnum to S2, where the filum terminale (an extension of the piamater beginning at the conus medullaris) blends with the periosteum of the subdural space which contains only small amounts of serous fluids to allow the duramater and arachnoidmater move over each other.

Surrounding the duramater is the epidural space which extends from the foramen magnum to the sacral hiatus. Posterior to the epidural space is the ligamentum flavum which extends from the foramen magnum to the sacral hiatus. Ligamentum flavum extends from the anterior inferior aspect

of the lamina above to the posterior superior aspect of the lamina below. Immediately posterior to the ligamentum flavum is the interspinous ligament. Extending from the external occipital protuberance to the coccyx, posterior to these structures is the supraspinous ligament.

Lumbar puncture is routinely done below the L2 vertebrae down to the L5-S1 interspace to avoid damaging the spinal cord which ends at the lower border of L1 in adults.

PHYSIOLOGY OF SUBARACHNOID BLOCK:

Cerebrospinal Fluid:

The cerebrospinal fluid (CSF) is an ultrafiltrate of blood plasma with which it is in hydrostatic and osmotic equilibrium. It is a clear, colorless fluid found in the spinal and cranial subarachnoid space and in the ventricles of the brain. The average volume in the adult ranges from 120-150 ml of which 35 ml is in the ventricles, 25 ml is in the cerebral subarachnoid space and 75 ml is in the spinal subarachnoid space. It is secreted by the choroid plexus at a rate of 0.3-0.4 ml/minute.

Physical Characteristics of Cerebrospinal Fluid:

pH	7.4
Specific gravity (H2O): At body temperature At 4 degree centigrade	 1.007 1.0003
Density	1.0003 g/ml
Baricity	1.000
Pressure	8-12 mm Hg/70-80 mm H2O
Cells	3-5/cu.mm
Proteins	20 mg/dl
Glucose	45-80 mg/dl

The cerebrospinal fluid plays an important role in spinal anesthesia as a media for dispersion of the local anesthetic drug to the spinal nerve. An important factor determining the spread of drugs in the subarachnoid space is the specific gravity of the injected solution compared with that of CSF.

Mechanism of Spinal Anaesthesia:

Injection of local anesthetic solution into the spinal CSF allows access to sites of action both within the spinal cord and the peripheral nerve roots. The nerve roots leaving the spinal canal are not covered by epithelium and

are readily exposed to the local anesthetic within the CSF. Therefore afferent impulses leaving via the ventral nerve roots are blocked during spinal anesthesia. Local anesthetics block sodium channels and electrical conduction in spinal nerve roots. There are also multiple potential actions of local anesthetics within the spinal cord at different sites. Local anaesthetics can exert sodium channel block within the dorsal and ventral horns, inhibiting generation and propagation of electrical activity.

Zone of Differential Blockade:

Sensory:

In Subarachnoid block, sympathetic fibres are two to three segments higher than sensory fibres. Sympathetic block will be greater when more concentrated solutions are used or when adrenaline is added, as this has a similar effect.

Motor:

In Subarachnoid block, the difference between sensory and motor block is slight (Two segments).

Order of blocking nerve fibers:

1. Autonomic preganglionic β fibers.
2. Temperature fibers- Cold before warm.
3. Pinprick fibers.
4. Fibers conveying pain greater than pin prick.
5. Touch fibers.
6. Deep pressure fibers.
7. Somatic motor fibers.
8. Fibers conveying vibratory sense and proprioceptic impulses.

During recovery, return of sensibility in the reverse order was assumed, but it has been suggested that sympathetic activity returns before sensation.

Spread of Local Anaesthetics in subarachnoid space:

Local anesthetic solution is diluted by CSF and therefore its original concentration is of less amount than the actual mass of drug injected. Spread is also determined by the baricity of the injected solution. Baricity is a ratio comparing the density of a local anesthetic solution at a specified temperature to the density of CSF at the same temperature. A hypobaric solution has a baricity less than 1.0000 or specific gravity less than

1.0069(the mean value of specific gravity). A hyperbaric solution has a baricity greater than 1.0000 or specific gravity more than 1.0069. Hypobaric and Hyperbaric solutions are prepared from isobaric solutions by the addition of various amounts of sterile distilled water and dextrose respectively. Isobaric solutions do not move under the influence of gravity in the CSF. Hyperbaric solutions, being heavier than CSF, settle to the most dependent aspect of the subarachnoid space, which is determined by the position of the patient. In supine patient, hyperbaric solutions gravitate to the thoracic kyphosis. Hypobaric solution floats up to the nerves innervating the surgical site. The major factors affecting height of the block are the baricity of the local anesthetic solution and the dosage of drug injected.

Fate of Local Anaesthetics in Subarachnoid Space:

Following injection of local anaesthetic solution into subarachnoid space, its concentration falls rapidly. The initial steep fall is due to mixing with CSF and subsequent absorption into nerve roots and spinal cord. The egress of local anesthetic solution following subarachnoid injection is primarily by vascular absorption with no hydrolysis or degradation taking place in the CSF. Depending on the type of the drug used, it is metabolized in plasma by pseudocholinesterase or in the liver.

Indications for subarachnoid block:

Spinal anesthesia can be administered whenever a surgical procedure can be done with a sensory level of anesthesia that does not produce adverse patient outcome which includes

- Lower abdominal surgeries
- Lower limb surgeries
- Urological procedures
- Obstetric procedures
- Gynecological surgeries
- Perineal and rectal surgeries

Contraindications for subarachnoid block:

An absolute contraindication for subarachnoid block is patient refusal.

Other contraindications are:

- Local sepsis
- Uncorrected coagulopathy
- Uncontrolled blood loss/shock
- Fixed cardiac output states
- Documented allergy to local anesthetics

- Raised intracranial pressure
- Neurological disease
- Major spine deformities/previous surgery on the spine
- Severe cardiac disease

Factors Influencing height of analgesia in Subarachnoid Block:

- Dose of the drug injected
- Volume of fluid injected
- Specific gravity of the solution
- Position of the patient during injection
- Posture of patient after injection
- Choice of interspace
- Patient factors- Age, Height, Pregnancy, Spinal stenosis

Factors not influencing height of analgesia in Subarachnoid Block:

- Patient factors- Weight, Sex
- Barbotage
- Speed of injection
- Composition and circulation of cerebrospinal fluid

- Direction of bevel of the standard needle (although not of the Whitacre needle)

Complications of subarachnoid block:

Immediate:

- Hypotension
- Bradycardia
- Toxicity due to intravascular injection
- Allergic reaction to local Anesthetic
- Hypoventilation (brain stem hypoxia)

Delayed:

- Post dural puncture headache
- Retention of urine
- Backache
- Meningitis
- Transient lesions of cauda equine
- Sixth nerve palsy
- Anterior spinal artery syndrome
- Horner's syndrome

Circulatory effects of subarachnoid block:

There are six different ways in which subarachnoid block can influence the cardiovascular system.

1. Vasodilatation of resistance and capacitance vessels.
2. Block of cardiac efferent sympathetic fibres from T1 to T4 resulting in loss of chronotropic and inotropic drive and fall in cardiac output.
3. The atrial or Bainbridge reflex causing bradycardia.
4. The operation of Marey's law causing tachycardia.
5. Depression of vascular smooth muscle and β-adrenergic blockade of myocardium with fall in cardiac output, following systemic absorption of the local anesthetic drug.
6. Adrenaline effect (if used), following absorption, resulting in β stimulation and associated rise in cardiac output and reduction in peripheral resistance. The overall effect is likely to be a greater fall in mean arterial pressure than if adrenaline had not been used.

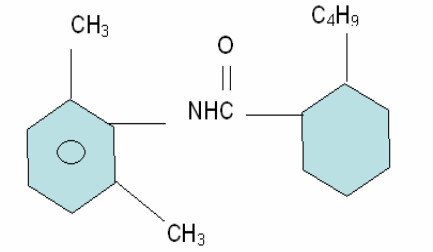
Theories of causation of fall in Blood pressure:

1. Diminished cardiac output consequent on reduction of venous return and lack of muscular propulsive forces on veins.

2. Dilatation of post arteriolar capillaries and small venules due to paralysis of vasoconstrictors.
3. Paralysis of Sympathetic nerve supply to the heart (T1-T4). Bradycardia may give rise to fall in cardiac output.
4. Paralysis of Sympathetic nerve supply to adrenal glands (Splanchnic nerves), with consequent catecholamine depletion.
5. Absorption of drug into circulation.
6. Ischaemia and hypoxia of vital centres.
7. Hypovolemia, if present, may give rise to severe fall in blood pressure if central neuraxial blockade is employed.
8. Compression of great vessels within the abdomen by the pregnant uterus, abdominal tumors or abdominal packs may cause severe hypotension in the presence of central neural blockade.

PHARMACOLOGY OF BUPIVACAINE

BUPIVACAINE



It is an amide local anaesthetic characterized as pipecoloxylidides.Addition of a butyl group to the piperidine nitrogen of mepivacaine results in Bupivacaine. It is a chiral drug because of possession of asymmetric carbon atom.

It was first synthesized in Sweden by **Ekenstam** and his colleagues in 1957 and used clinically by **L.J.Telivuo** in 1963. Its molecular weight is 288.

MECHANISM OF ACTION

It prevents transmission of nerve impulses by inhibiting passage of sodium ions through ion selective sodium channels in nerve membranes. They do not alter the resting transmembrane potential or threshold potential.

PHARMACOKINETICS

It is a weak base that has pk value above physiologic pH. At pH 7.4 only 15% exists in nonionised form. Absorption depends on the site of injection, dosage and use of epinephrine. Lung is capable of extracting bupivacaine from circulation, which will limit concentration of drug that reaches systemic circulation. This first pass pulmonary extraction is dose dependent suggesting that it becomes saturated rapidly.

Pk	:	8.1
Protein Binding	:	95%
Lipid solubility	:	28
Volume of distribution	:	73 litre
Clearance of drug from plasma	:	0.471 lit/min
Elimination half life	:	210 min (3.5 hours)
Onset time	:	5 -7 min

METABOLISM

Slowest metabolism among amide local anaesthetics. It undergoes aromatic hydroxylation, N- dealkylation, amide hydrolysis and conjugation. Only the N-desbutyl bupivacaine has been measured in blood or urine after epidural or spinal anaesthesia. Alpha-1 acid glycoprotein is the most important protein-binding site of bupivacaine.

SIDE EFFECTS

Bupivacaine is more cardio toxic than equieffective doses of lignocaine. This is manifested by severe ventricular arrhythmias and myocardial depression. Bupivacaine blocks cardiac Na+ channels rapidly during systole and dissociates more slowly during diastole, so that a significant fraction of Na+ channels remain blocked at the end of the diastole. Thus the block by Bupivacaine is cumulative and substantially greater.

CLINICAL USE

Onset of anaesthesia and duration of action are long. Its tendency to provide more sensory than motor block has made it popular for providing postoperative analgesia. Used mainly for

- Infiltration anaesthesia
- Field block anaesthesia
- Nerve block anaesthesia
- Spinal anaesthesia
- Epidural anaesthesia

PHARMACOLOGY OF FENTANYL

Fentanyl is a synthetic phenylpiperidine opioid of the 4-anilopiperidine series which is structurally related to pethidine.

Commercially, fentanyl is formulated as a citrate, available as an aqueous solution without preservatives. Each ml contains a base of 50mcg of fentanyl.

PHYSICOCHEMICAL PROFILE

Molecular weight	528.29
pKa	8.4
% unionized at pH 7.4	8.5 %
Octanol / water partition coefficient	816
% bound to plasma proteins	84 %
Potency	80 times more potent than morphine

PHARMACODYNAMICS

Analgesia

Analgesia results from action of fentanyl on opoid mu receptors both supraspinally in the brain and in the spinal cord. Intravenous fentanyl produces effective analgesia at plasma concentrations between 0.6 - 3.0 ng/ml.

Cardiovascular system

Arterial blood pressure, cardiac output and pulmonary vascular resistance remain unchanged after large doses of intravenous fentanyl. Fentanyl like other opioid agonists (except pethidine) causes bradycardia, that responds to intravenous atropine. Peripheral vasodilation is much less than morphine due to absence of histamine Release.

Respiratory System

Fentanyl causes a direct dose related respiratory depression by its depressant effect on the medullary respiratory centre, manifested as a decreased sensitivity to Carbondioxide and reduced respiratory rate. It is reversed by intravenous Naloxone administration. Plasma fentanyl concentrations >2ng/ml is associated with clinical respiratory depression.

The degree of respiratory depression is affected by various factors, including type of surgery, age and individual pharmacodynamic response.

Central nervous system

Fentanyl causes less sedation than equianalgesic doses of morphine . In doses of 10 mcg/kg , fentanyl causes dose related reduction in cerebral blood flow and CMRO2. Muscle rigidity probably reflects a manifestation of a catatonic state, a basic pharmacological property of opioids, related to enhancement of dopamine biosynthesis in the caudate nucleus.

Gastrointestinal Tract

Fentanyl decreases gastrointestinal tract motility, increases intrabiliary pressure and causes a varying incidence of nausea and vomiting. The vomiting is mediated via stimulation of the chemoreceptor trigger zone in the area postrema.

Genito-urinary system

Fentanyl like other opioids causes relaxation of the detrusor muscle and increase in the urethral sphincter tone leading to urinary retention. This

is probably not dose related and is more common with central neuraxial administration.

Pharmacokinetics

Fentanyl is a potent opioid, highly lipophilic, producing a rapid onset of action of relatively short duration. After intravenous administration, fentanyl is rapidly distributed to brain, heart and other highly perfused tissues. It also crosses the placental barrier easily. Peak effect occurs in 5 minutes. Within a short time, the drug redistributes to the inactive tissues sites like skeletal muscle and fat, associated with decrease in plasma concentration of drug, thus terminating its effect. About 75% of initial dose undergoes first pass pulmonary uptake. When low doses(1-2mcg/kg) are administered, redistribution terminates the effect and the drug appears short acting. With administration of large intravenous doses or continous infusion, progressive saturation of inactive tissue sites occur.

Pharmacokinetic Profile

Volume of distribution at steady state(VDss)	335litres
Clearance	1530 ml/min
Effect- site equilibration time	6.8 min

Hepatic extraction ratio	0.8-0.1
Context – sensitive half time (4 hrs infusion)	260 mins
Elimination half time	3.1 to 6.6 hours

Metabolism

Fentanyl is biotransformed in the liver to inactive metabolites, primarily Norfentanyl and several hydroxylation products. Only 4-7% of drug is excreted unchanged in the urine. Elimination half time of fentanyl is longer than that of morphine because of the high lipid solubility of fentanyl. Eliminition half time is prolonged in elderly Patients. A high hepatic extraction ratio means that the clearance of fentanyl is limited by hepatic blood flow.

ROUTES OF ADMINISTRATION AND DOSAGE

Intramuscular

50-100mcg may be administrated as premedication 30-60 minutes prior to surgery.

Intravenous

Can be given intraoperatively and postoperative analgesia. Postoperative analgesia is achieved by intravenous loading dose of 1-2mcg/kg followed by

a Continous / variable infusion at rate of 1-2 mcg/kg/hr. It can be used for Patient-Controlled analgesia (PCA) as a bolus dose of 20-50mcg with lockout intervals.

Transdermal

Transdermal fentanyl patch is available in four sizes, providing sustained release of fentanyl at rates of 25, 50, 75 and 100mcg/hr for periods of 48-72 hours. Skin acts as a secondary reservoir contributing to prolonged residual fentanyl concentrations.

Transmucosal

Oral transmucosal fentanyl citrate (OTFC) incorporates fentanyl citrate in a candy mixture shaped into a lozenges or stick. The median time to onset of analgesia is 4 minutes and the duration of analgesia lasts for about 150 minutes.

Intranasal

Fentanyl is administered with a metered dose device, with each spray delivering 4.5mcg fentanyl. Time to onset of analgesia is about 15 minutes.

Transpulmonary

Inhalational administration of fentanyl produces rapid, effective drug delivery. A dose of 300mcg of fentanyl administered via oxygen driven nebuliser produces effective postoperative analgesia in 5 mins and lasts for about 2 hours.

Neuraxial administration

Epidural and intrathecal administration of fentanyl are long stablished routes for intraoperative and postoperative analgesia. Epidural dose as a single bolus administration varies from 1-3 mcg/kg. Analgesia begins in 15 minutes lasting for 2-4 hours. Epidural infusion rates range from 0.5-2.5mcg/kg/h. In addition, fentanyl has been used in Patient controlled epidural Analgesia(PCEA) in doses of 20-25mcg with a lockout interval of 6-10mins and background infusion in the rate 0.5-1mcg/kg/h.The minimum intrathecal bolus requirement for postoperative analgesia is 20mcg while a dose of 10mcg is effective in obstetric patients. Onset of analgesia is usually within 5-15 mins and duration is variable, ranging from 1-5 hours. Other modes of administration include continous / bolus administration via an intrathecal Catheter.

Clinical Applications

Premedication

Fentanyl in doses of 50- 100mcg may be administered intramuscularly 30-60 minutes prior to surgery. Oral transmucosal fentanyl citrate in doses between 15-20mcg/kg, administered 45 minutes before surgery produces reliable preoperative sedation and facilitates induction of anaesthesia in children.

Adjunct to general anaesthesia.

Fentanyl in doses of 1-2mcg/kg given intravenously provides analgesia. It can be used as an adjuvant to blunt circulatory responses that occur during direct laryngoscopy for endotracheal intubation and sudden changes in the level of surgical stimulation . Large doses of fentanyl, 50-150mcg/kg intravenously has been used especially in cardiothoracic procedures, principally because of its stable hemodynamic effects.

Neurolept analgesia

Innovar is a premixed combination containing 2.5 mg Droperidol and 0.05mg Fentanyl in each ml (50:1) used for neurolept analgesia and anaesthesia.

Adjunct in central neuraxial block

Fentanyl added to local anaesthetic either intrathecally or epidurally, improves the quality of intraoperative analgesia and also provides good post operative Analgesia.

Postoperative analgesia

Fentanyl administration by intravenous, epidural, intrathecal and transdermal routes provides effective postoperative analgesia. Newer routes like intranasal and inhalational administration are being evaluated as less invasive means of postoperative analgesia.

Side effects

Commonly occurring side effects include dose dependant respiratory depression, muscle rigidity, nausea and vomiting, pruritus, urinary retention and bradycardia. These effects are reversed by administration of naloxone intravenously.

Intrathecal fentanyl

Intrathecal fentanyl administration is an established route for intraoperative and postoperative analgesia.

Pharmacokinetics

Fentanyl has the same baricity as cerebrospinal fluid at room temperature and addition to hyperbaric lignocaine or bupivacaine makes the solution hyperbaric. On injection into subarachnoid space, fentanyl mixes with csf and attaches itself to spinal opioid receptors. Protein binding of drug in the CSF is negligible and the concentration of opioid in the csf is thus free drug concentration. CSF dynamics donot provide any means of drug removal. Diffusion into the spinal cord and absorption into the blood flowing through spinal cord must remove all the fentanyl. This rate determining step of drug removal is likely to be the rate constant for fentanyl transfer from csf to spinal cord and this rate constant is directly related to lipophilicity. Fentanyl can also migrate from the csf into epidural vascular compartment via the duramater. However details of systemic pharmacokinetics of fentanyl are not known. Once in the csf, fentanyl like other opioids, spreads rostrally. Because of the high affinity of fentanyl with binding sites in the lipid-rich Spinal cord, only 10% of administered dose migrates to cervical region.

Application

Intrathecal fentanyl is usually combined with local anaesthetics for perioperative anaesthesia and analgesia particularly in obstetrics. Fentanyl administration intrathecally provides more intense and complete analgesia at rest, at a lower dose requirement when compared to the epidural or intravenous routes.

Modes of administration and dosages

Fentanyl is administered intrathecally as single bolus injection or as repeated observer-administered, PCA boluses and continous infusion via an intrathecal catheter. Effective postoperative analgesia can be achieved with bolus doses of 20mcg. Infusions of 0.8mcg/kg/h produces satisfactory analgesia in patients undergoing thoracotomy.

Side effects of intrathecal fentanyl

Side effects are relatively minor with intrathecal fentanyl. The incidence of clinically significant respiratory depression is relatively low, as Intrathecal administration of fentanyl results in lower systemic absorption than epidural route and the intrathecal dose requirement. A 30% incidence of urinary retention, varying incidence of pruritus and occasional episodes of nausea have been observed

PHARMACOLOGY OF MAGNESIUM

It is a bivalent ion like calcium with an atomic weight of 24.312. Human body contains 1 mole (24g) of magnesium. It is the fourth common mineral salt in the body after phosporus, calcium and potassium, second intracellular cation after potassium. In serum, magnesium is divided into three fractions-

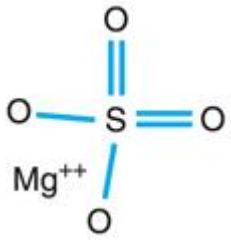
1) Ionised,

2) Protein bound and

3) Contained in anion complexes.

These fractions account for 65%, 27%, and 8% in serum concentration respectively.

CHEMICAL STRUCTURE OF MAGNISIUM SULPHATE:



Magnesium sulphate

PROPERTIES OF MAGNESIUM SULPHATE:

1) CELLULAR PROPERTIES:

Magnesium intervenes in the activation of membrane calcium ATPase and Na+ K+ ATPase involved in transmembrane ion exchange during depolarization and repolarization phases. It acts as a stabilizer of cell membrane and intracytoplasmic organelles.

2) ION CHANNELS:

It acts as a regulator of different ion channels. It has a competitive antagonist action against calcium inflows thereby limiting the outflow of calcium from the sarcoplasmic reticulum. So it is a calcium channel blocker and calcium channel modulator.

3) CARDIOVASCULAR SYSTEM:

It acts on calcium channels in the myocardial muscle and also acts indirectly on the cardiac muscle by inhibiting the calcium uptake on the Troponin C of the myocytes and thereby influencing myocardial contractility.

Its vasodilatory action is due to its activation of cyclic AMP. This causes reduction in systolic blood pressure.

Pulmonary vascular resistance is unaltered.

Coronary vascular resistance is reduced and causes vasodilation.

4) NEUROMUSCULAR TRANSMISSION:

It has a preponderant presynaptic and postsynaptic effect. Magnesium acts competitively in blocking the entry of calcium into the presynaptic endings. Presynaptic release of acetylcholine is reduced by magnesium, thereby decreasing the effect of acetylcholine on the postsynaptic receptors, which in turn increases the threshold of axonal excitation.

It also produces progressive inhibition of catecholamine release from the adrenal medulla, adrenergic nerve endings and adrenergic postganglionic sympathetic fibers.

5) RESPIRATORY SYSTEM:

It has bronchodilatory action due to the inhibition of smooth muscle contraction, histamine release from the mast cells and acetylcholine release from the cholinergic nerve endings.

6) It is involved in hundreds of enzyme reactions in the body.

7) Acts as a antagonist of NMDA receptors and this explains its use in Post-operative analgesia.

8) Magnesium sulphate increases production of prostaglandins causing vasodilatation of the small intracranial vessels which is responsible for its anticonvulsant action.

CLINICAL USES:

1) For Severe Preeclampsia and Eclampsia:

A loading dose of 4-6gm magnesium sulphate diluted in 100ml of normal saline given over 15min intravenously. Then 2 gm/hr in 100ml of IV infusion. (maintain serum levels between 4 and 7mEq/L).

Intermittent injection:

4gm given slow IV followed by 10gm, 5gm in each buttocks as deep IM injection. Then every 4hrs 5gm intramuscularly upto 24hrs after delivery.

2) Magnesium sulphate has a tocolytic effect at serum levels of 8-10mEq/L. Loading dose of 4-6gm over 20min intravenously, then after the contraction ceases maintenance is done using 2-4gm per hour intravenously for 12-24 hours.
3) To reduce the stress response during intubation, magnesium sulphate is used in the dosage of 30-50mg/kg. intravenously.
4) In surgery for Phaeochromocytoma it helps to maintain haemodynamic balance because it inhibits the catecholamine release from adrenal medulla and adrenergic nerve endings.
5) Nephritic Seizures: In children with nephritic seizures, the 50% concentration should be diluted to a 20% solution for i.m. injection. The

dose for children is 20 to 40 mg (0.1 to 0.2 mL of a 20% solution)/kg of body weight, administered i.m. as needed, to control seizures.

6) It is used postoperatively in patients who have undergone Coronary artery bypass grafting to reduce the incidence of ventricular arrhythmias.
7) It is also used in the treatment of Torsades De Pointes, as intravenously or intraosseously in the dosage of 25 to 50 mg/ kg (upto 2 gm).
8) Acute myocardial infarction: magnesium sulphate is used in the dose of 2gm intravenously over 5-15 min followed by 18 gm over 24hrs as infusion.
9) Total Parenteral Nutrition: In total parenteral nutrition, maintenance requirements for magnesium are not precisely known. The maintenance dose recommended for adults is 5 to 8 mEq magnesium/L of TPN solution; typical daily adult intake ranges from 10 to 24 mEq. For infants, the recommended intake ranges from 0.25 to 0.6 mEq/kg/day.
10) In barium poisoning: 1-2gm is used to counteract the intense muscle stimulating effects of barium.
11) In refractory bronchial asthma it is used for its bronchodilatory action.
12) Hypomagnesemia: in case of mild deficiency 1gm every 6 hours for 4 doses, in severe cases 1-5gms (2 – 10ml of 50% solution) in divided doses, repeated until the serum levels are normal.

13) Recent studies show its use in Tetanus patients, at a serum concentration of 2-4mEq/L, it gives good control of spasms and muscle rigidity.

14) Magnesium sulphate is used in the dose of 50 mg intrathecally for potentiation of opioid analgesia.

PRECAUTIONS:

Because magnesium is removed from the body solely by the kidneys, the drug should be used with caution in patients with renal impairment. Urine output should be maintained at a level of 25 - 50 ml per hour. Monitoring serum magnesium levels and the patient's clinical status is essential to avoid the consequences of over dosage in toxemia. Clinical indications of a safe dosage regimen include the presence of the patellar reflex (knee jerk) and absence of respiratory depression (approximately 16 breaths or more/minute). Serum magnesium levels usually sufficient to control convulsions range from 3 to 6 mg/100 ml (2.5 to 5.0 mEq/L). The strength of the deep tendon reflexes begins to diminish when magnesium levels exceed 4 mEq/L. Reflexes may be absent at 10 mEq magnesium/L, where respiratory paralysis is a potential hazard. An injectable calcium salt

should be immediately available to counteract the potential hazards of magnesium intoxication in eclampsia.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not administer unless solution is clear and container is undamaged. Discard unused portion.

PREPARATIONS AVAILABLE:

Parenteral injection: Magnesium sulphate-	10%, 12.5%, 50%
For Intravenous use only-	4%, 8%.
Magnesium sulphate in dextrose:	1% in 5%dextrose.
	2%in 5% dextrose.

When administered intravenously the onset of action is immediate and duration of action is 30 min. on administration by intramuscular route the onset of action takes 1hr and duration of action is 3-4 hrs.

Storage: 15-30degree centigrade. For IV use concentration of 20% or less should be used. Rate of injection should be 1.5ml/hr.

DRUG INTERACTIONS:

Central nervous system depressants: When barbiturates, opiates, general anaesthetics, or other CNS depressants are administered concomitantly with magnesium sulfate, dosage of these agents must be carefully adjusted because of the additive central depressant effects.

Neuromuscular blocking agents: Excessive neuromuscular blockade has occurred in patients receiving parenteral magnesium sulfate and a neuromuscular blocking agent; these drugs should be administered concomitantly only with caution.

Cardiac glycosides: Magnesium salts should be administered with extreme caution in digitalized patients, because serious changes in cardiac conduction, which can result in heart block may occur if administration of calcium is required to treat magnesium toxicity.

ADVERSE REACTIONS:

The adverse effects of parenterally administered magnesium usually are the result of magnesium intoxication. These include flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac and CNS depression proceeding to respiratory paralysis.

Hypocalcemia with signs of tetany secondary to magnesium sulphate therapy for eclampsia, has been reported.

SYMPTOMS AND TREATMENT OF OVERDOSE:

Magnesium intoxication is manifested by a sharp drop in blood pressure and respiratory paralysis. Disappearance of the patellar reflex is a useful clinical sign to detect the onset of magnesium intoxication. In the event of overdosage, artificial ventilation must be provided until a calcium salt can be injected i.v. to antagonize the effects of magnesium.

In adults, i.v. administration of 5 to 10 mEq of 10% calcium gluconate will usually reverse respiratory depression or heart block due to magnesium intoxication. In extreme cases, peritoneal dialysis or hemodialysis may be required

Hypermagnesemia in the newborn may require resuscitation and assisted ventilation via endotracheal intubation or intermittent positive pressure ventilation, as well as i.v. calcium.

MATERIALS AND METHODS

After approval of the study by our institutional ethics committee, the study was conducted in 50 ASA grade I or II patients undergoing elective lower abdominal surgeries under spinal anaesthesia. The age of the patients ranged from 23– 68 years weighing 35 – 65 kg and height ranging from 150 – 168 cms. All patients were thoroughly examined preoperatively.

Informed written consent was obtained and the procedure was explained. For all patients age, weight, heights were noted.

In the assessment room, vital parameters like pulse rate, blood pressure and baseline investigations like hemoglobin, urine analysis for albumin and sugar, blood sugar, urea and creatinine and ECG were checked. Thorough examination of all the systems and airway assessment was done.

Exclusion criteria included significant co existing disease, long term opioid use, any contraindications to regional anaesthesia such as local infection or bleeding disorders. Visual Analog Scale (VAS) was explained to the patients. The patients were shown a 10 cm long scale marked 0 – 10 on a blank paper and told that 0 represented “no pain” and 10 represented worst possible pain.

The patients were randomly allocated into two groups of 25 each.

GROUP S

Patients received 2 ml 0.5% bupivacaine (10 mg)

0.5 ml fentanyl (25 mcg)

1 ml normal saline

GROUP M

Patients received 2 ml 0.5% bupivacaine (10 mg)

0.5 ml fentanyl (25 mcg)

1 ml MgSO4 (50 mg)

The total volume of the injected solution was 3.5 ml in both groups. In the operating room, appropriate equipment for airway management and emergency drugs were kept ready. Patients were shifted to the operating room. The horizontal position of the operating table was checked and the patients were positioned. Noninvasive blood pressure monitor, pulse oximeter and ECG leads were connected to the patient. Preoperative baseline systolic and diastolic blood pressure, pulse rate and oxygen saturation were recorded. Patients were cannulated with 18 G intravenous cannula and preloaded with 1000 ml of ringer lactate. The patient was placed in right lateral position. The skin over the back was prepared with antiseptic solution and draped with sterile towel. Lumbar puncture was performed with a 25G Quincke babcock spinal needle at L2 – L3 or L3 – L4 interspace via midline

approach. After confirming free flow of CSF, the prepared solution was injected.The patients were made to lie supine immediately after injection and the time at which the spinal anaesthesia performed was noted.

The following parameters were observed:

SENSORY BLOCK

The onset of sensory block was defined as the time between the injection of anaesthetic solution and the absence of pain at the T10 dermatome. Sensory block was assessed by loss of sensation to pinprick using 21G sterile needles bilaterally along the mid clavicular line. This assessment started immediately after turning the patient supine and continued every minute till loss of sensation to pinprick at T 10 level was noted. This pinpricking continued till the peak block height was reached and the time was noted. The duration of sensory block was defined as the time for regression of two segments from the maximum block height evaluated by pin prick. Sensory block was checked every 15 mins till it reached two segment regression levels.

MOTOR BLOCK

Motor block was assessed bilaterally using Modified bromage scale.

MODIFIED BROMAGE SCALE.

0 - No block. Able to raise extended legs against gravity.

1 - Unable to raise extended leg, but just able to flex knees.

2 - Unable to flex knees but able to flex ankle.

3 - Total block. Inability to flex ankle / move leg.

Assessment of motor block was started immediately after turning the patient supine and continued every minute till bromage score of 1 was reached. The onset of motor block was defined as the time to achieve bromage score of 1 from the time of injection. Duration for complete motor block recovery was taken as the time from subarachnoid injection to return of bromage score of 0.

VITAL SIGNS AND SIDE EFFECTS

Systolic and diastolic blood pressure, pulse rate and oxygen saturation were recorded every 2 mins for the first 10 mins and thereafter every 5 mins until the immediate postoperative period. Hypotension was defined as fall in systolic blood pressure more than 30 % from baseline or systolic blood

pressure less than 90 mm Hg. This was managed with intravenous ephedrine in incremental dose of 6 mg.

Bradycardia was defined as heart rate less than 60 / min and was planned to be managed with intravenous atropine in incremental doses. Respiratory depression was said to be present if respiratory rate was less than 8 per minute and / or SpO_2 than 85 %. This was planned to be managed with mask ventilation or intubation and IPPV. Vomiting was planned to be managed with Inj. Odansetron 8 mg intravenously. Pruritis was planned to be managed with reassurance or inj. Pheniramine maleate 22.75 mg intravenously. Urinary retention was monitored postoperatively and catheterization was planned in patients with retention more than 6 hours. Patients were shifted to post anaesthesia care unit after completion of surgery. Vital signs were recorded every 15 mins in the first hour after surgery, 30 mins for the next 2 hours and thereafter every hour for the next 3 hours. Motor block was assessed till bromage score of 0 was reached. Patients were shifted to postoperative ward after complete resolution of motor blockade and stabilization of blood pressure.pain assessment was done using VAS every 15 mins till VAS score of 4 was reached. The VAS was also noted whenever the patient complained of pain. Inj.Diclofenac sodium 75 mg was given intramuscularly as the rescue analgesic when VAS

of 4 or more was reached. Patients were monitored for 24 hours to detect side effects like respiratory depression, urinary retention, pruritis, nausea and vomiting.

DURATION OF ANALGESIA

The time at which the patient first complained of pain was noted. The duration of effective analgesia was defined as the period from the spinal injection to the first occasion when the patient complained of pain in the postoperative period.

OBSERVATION AND ANALYSIS

Of the fifty patients, 25 belonged to group S and other 25 belonged to group M.

AGE DISTRIBUTION

The age distribution in group S was 24 to 65 years while in group M was 23 to 68 years. The mean age and age distribution in both groups were Statistically similar (p value 0.949) which is as under

AGE IN YEARS	GROUP S	GROUP M
MINIMUM	24	23
MAXIMUM	65	68
MEAN	41.36	41.92

SEX DISTRIBUTION

Of the 50 pts, 27 were male and 23 were female. The distribution was similar in both the groups as shown by the table and bar diagram.

SEX	GROUP S	GROUP M
MALE	14	13
FEMALE	11	12
TOTAL	25	25

WEIGHT DISTRIBUTION

The mean weight of the patients in both the groups were comparable (p value 0.616).

WEIGHT IN KG	GROUP S	GROUP M
Range	35 - 64	35 - 65
Mean	47.96	47.28

HEIGHT DISTRIBUTION

The mean height was also statistically comparable in both the groups (p value 0.837).

HEIGHT IN CM	GROUP S	GROUP M
Range	**150 - 164**	**150 - 168**
Mean	**155.76**	**155.32**

SENSORY BLOCKADE

SENSORY BLOCKADE (IN MINS)	GROUP S	GROUP M	P VALUE
ONSET	**4.28 ± 0.98**	**4.48 ± 0.96**	**0.470**

MOTOR BLOCKADE

MOTOR BLOCKADE (IN MINS)	GROUP S	GROUP M	P VALUE
ONSET	5.08 ± 0.86	5.24 ± 0.78	0.494
TIME FOR COMPLETE MOTOR RECOVERY	130.36 ± 10.4	131.4 ± 10.5	0.936

DURATION OF ANALGESIA

The mean duration of effective analgesia was 141.48 ± 11 mins with a range of 120 – 161 mins in group S but in group M it was 154.56 ± 11.1 mins with a range of 133 – 174 mins. The probability value, as detected by two sample students "t" test is 0.083.

	GROUP S	GROUP M	P VALUE
DURATION OF ANALGESIA (IN MINS)	141.48 ± 11	154.56 ± 11.1	0.083

PARAMETERS	MEAN ± S.D		P VALUE
	GROUP S	GROUP M	
AGE	41.36 ± 12.9	41.92 ± 13.4	0.949
HEIGHT	155.76 ± 4.68	155.32 ± 4.89	0.837
WEIGHT	47.96 ± 10.5	47.28 ± 7.79	0.616
ONSET OF SENSORY BLOCK	4.28 ± 0.98	4.48 ± 0.96	0.470
ONSET OF MOTOR BLOCK	5.08 ± 0.86	5.24 ± 0.78	0.494
DURATION FOR COMPLETE MOTOR RECOVERY	130.36 ± 10.4	131.4 ± 10.5	0.936
DURATION OF ANALGESIA	141.48 ± 11	154.56 ± 11.1	0.083

SIDE EFFECTS	GROUP S	GROUP M
NAUSEA AND VOMITING	4	3
SHIVERING	3	3
PRURITIS	5	6
URINARY RETENTION	3	4
BRADYCARDIA	-	-
RESPIRATORY DEPRESSION	-	-
HYPOTENSION	12	13

REVIEW OF LITERATURE

M.OZALEVLI et al had done a study about the effect of adding intrathecal magnesium sulphate to bupivacaine and fentanyl in patients undergoing lower extremity surgeries. Group S, the saline group received 2 ml 0.5% bupivacaine (10 mg) 0.5 ml fentanyl (25 mcg) and 1 ml normal saline intrathecally. Group M received 2 ml 0.5% bupivacaine (10 mg) 0.5 ml fentanyl (25 mcg) and 1 ml MgSO4 (50 mg) intrathecally. The total volume of the injected solution was 3.5 ml in both groups .The onset of sensory blockade was delayed in Group M (12 mins in group s vs 17 mins in group m). The duration of sensory block was similar in both groups (85 mins in both groups).The onset of motor blockade was delayed in group M (16 mins in group S vs 20 mins in group M).The study explained the probable reason for the delay in onset that the solution to which magnesium sulphate was added had a different pH. The duration of spinal analgesia was longer in group M (155 mins in group S vs 173 mins in group M). The mechanism they cited was magnesium sulphate , as an NMDA antagonist has prevented central sensitization due to peripheral nociceptive stimulation.The incidence of side effects were similar in both the groups.The study concluded that magnesium sulphate when added intrathecally to

bupivacaine and fentanyl delayed the onset of both sensory and motor blockade but prolonged the period of analgesia without increasing the incidence of side effects.

BUVENDRAN et al conducted a study evaluating whether intrathecal magnesium could prolong spinal opioid (fentanyl) analgesia in patients requiring labour analgesia. Patiets were allocated into two groups. Group F received 0.5 ml fentanyl (25 mcg) and 3 ml normal saline whereas Group F+ M received 0.5 ml fentanyl (25 mcg) and 3 ml magnesium sulphate (50 mg) . The duration of spinal analgesia was longer in Group F+ M (75 mins) compared with group F (60 mins). There were no differences in the demographic characteristics, hemodynamic parameters and foetal heart rate.

KROIN et al demonstrated that magnesium sulphate potentiates morphine analgesia when administered intrathecally in normal rats and suggested that intrathecal magnesium sulphate may be a useful adjuvant to spinal morphine analgesia. Histological evaluation of the spinal cord showed identical histologic changes with the control group and the animals had no neurological deficit. They demonstrated that intrathecal magnesium sulphate has a safety profile.

SIMPSON et al studied intrathecal magnesium sulphate effect in dogs undergoing thoracic aortic cross clamping via small thoracotomy incision and concluded that intrathecal magnesium sulphate can prevent spinal cord injury. None of the histological specimens from dogs that received magnesium exhibited any histologic evidence of ischaemic and neurological injury. This study also demonstrates the safety profile of intrathecal magnesium sulphate.

DISCUSSION

The primary aim of this study was to evaluate the effect of adding magnesium sulphate to bupivacaine and fentanyl spinal anaesthesia. The safety of intrathecal magnesium sulphate administration in humans and animals have been established. **SIMPSON et al** and **KROIN et al** demonstrated in animals that intrathecal magnesium sulphate has a safety profile. Histological evaluation of the spinal cord showed identical histologic changes with the control group and the animals had no neurological deficit. **M.OZALEVLI et al and BUVENDRAN et al** demonstrated no deleterious effects in humans on administration of intrathecal magnesium sulphate.

The dose of magnesium sulphate used in this study was based on data from **M.OZALEVLI et al and BUVENDRAN et al** where 50 mg of magnesium sulphate potentiated opioid analgesia. The dose of magnesium sulphate was based on data from a rat model of postoperative pain in which 188 micrograms of intrathecal magnesium sulphate potentiated morphine antinociception done by **KROIN et al.** Based on the relative differences between human and rat CSF volume and body weight, the 188 microgram dose was conservatively extrapolated to 50 mg for humans.

SENSORY AND MOTOR BLOCKADE

The time to onset of motor blockade was 5.08 ± 0.86 mins in group S and 5.24 ± 0.78 mins in group M (p value 0.494)which means that both the groups showed no statistical difference in onset.

The time to achieve complete recovery of motor blockade was130.36 ± 10.4 mins in group S and was 131.4 ± 10.5 mins in group M (p value 0.936) which shows that the duration of motor blockade was similar in both the groups.

The mean time to sensory onset at T 10 was 4.28 ± 0.98 mins in group S and 4.48 ± 0.96mins in group M (p value 0.470**).** This implies that the onset of sensory block was similar in both the groups.

DURATION OF EFFECTIVE ANALGESIA

The mean duration of effective analgesia was 141.48 ± 11 mins with a range of 120 – 161 mins in group S but in group M it was 154.56 ± 11.1 mins with a range of 133 – 174 mins. The probability value as detected by two sample students "t" test is 0.083. This implies that addition of intrathecal magnesium sulphate to bupivacaine and fentanyl prolonged the period of analgesia but the potentiation was not statistically significant in our study.

This correlates with the study done by **M.OZALEVLI et al** who concluded that addition of intrathecal magnesium sulphate to bupivacaine and fentanyl prolonged the period of analgesia.

This also correlates with the study done by **BUVENDRAN et al** who concluded that magnesium sulphate when administered intrathecally prolonged the duration of spinal opioid analgesia in humans.

SIDE EFFECTS

The incidence of nausea and vomiting was 16 % in group S and 12% in group M. The incidence of shivering was similar in both the groups (12 %) The incidence of pruritis was 16 % in group S and 12% in group M. The incidence of urinary retention was 16 % in group S and 12% in group M. Hypotension occurred in 48% of the patients in group S and 52% of the patients in group M.

From the above findings it is clear that the incidence of side effects were similar in both the groups.

SUMMARY

We conducted a double blinded randomized controlled study in 50 patients belonging to ASA I and II undergoing elective lower abdominal surgeries to evaluate the effect of adding intrathecal magnesium sulphate to bupivacaine and fentanyl. For the same reason , we divided randomly the patients into two groups of 25 each.

Group S received 2 ml 0.5% bupivacaine (10 mg) ,0.5 ml fentanyl (25 mcg) and 1 ml normal saline .

Group M received 2 ml 0.5% bupivacaine (10 mg) ,0.5 ml fentanyl (25 mcg) and 1 ml MgSO4 (50 mg).

The total volume of the injected solution was 3.5 ml in both groups. The onset of sensory and motor blockade, the duration of sensory and motor blockade and the duration of analgesia were noted in both the groups. Demographic data were similar in both the groups.

We found that the onset of sensory and motor blockade was similar in both the groups . The duration of sensory and motor blockade was also similar in both the groups.

The duration of analgesia was prolonged in the magnesium sulphate group but the potentiation was not significant in our study.

The incidence of side effects were similar in both the groups .

CONCLUSION

This study concludes that intrathecal magnesium sulphate when added to bupivacaine and fentanyl prolonged the period of analgesia but not significantly in patients undergoing elective lower abdominal surgeries without increasing the incidence of side effects.

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PROFORMA

THE EFFECT OF ADDING INTRATHECAL MAGNESIUM SULPHATE TO BUPIVACAINE – FENTANYL SPINAL ANAESTHESIA IN PATIENTS UNDERGOING LOWER ABDOMINAL SURGERIES

DATE

NAME AGE SEX

IP NO HEIGHT WEIGHT

DIAGNOSIS SURGERY

PREANAESTHETIC EVALUATION

HISTORY

NIL ORAL FROM

PR BP

CVS RS OTHER SYSTEMS

AIRWAY ASA GRADE

ANAESTHESIOLOGIST SURGEON

INVESTIGATIONS

Hb URINE ALBUMIN

SUGAR

BLOOD SUGAR UREA CREATININE

CXR ECG

PRELAODING

INTRATHECAL INJECTION

POSITION

INTERSPACE

NEEDLE

TIME OF INJECTION OF ANAESTHETIC SOLUTION

ONSET OF SENSORY BLOCK AT T10

PEAK SENSORY LEVEL

TWO SEGMENT REGRESSION TIME

ONSET OF MOTOR BLOCK

MAXIMUM GRADE OF MOTOR BLOCK

DURATION FOR COMPLETE MOTOR RECOVERY

DURATION OF EFFECTIVE ANALGESIA

INTRAOPERATIVE MONITORING

PR

BP

SPO2

DRUGS

EVENTS

IV FLUIDS

POSTOPERATIVE MONITORING

TIME IN MINS	0	15	30	45	60	90	120	180	240	300	360
PR											
BP											
SPO2											
VAS											

SIDEEFFECTS **TREATMENT**

PRURITIS

NAUSEA AND VOMITING

RESPIRATORY DEPRESSION

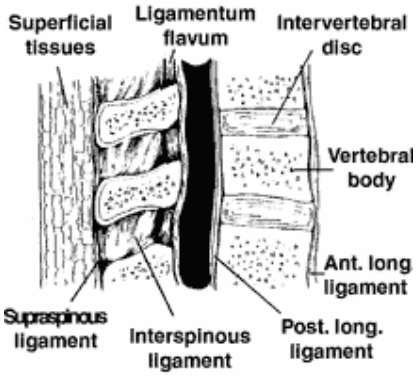
URINARY RETENTION

HYPOTENSION

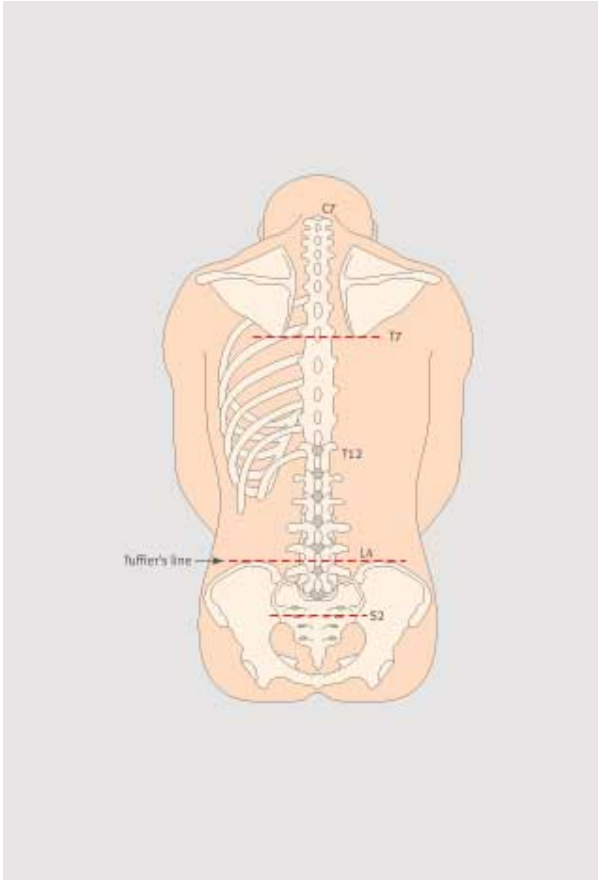
OTHERS

SUPERVISING ANAESTHESIOLOGIST PROFESSOR AND HOD

DEPT OF ANAESTHESIOLOGY

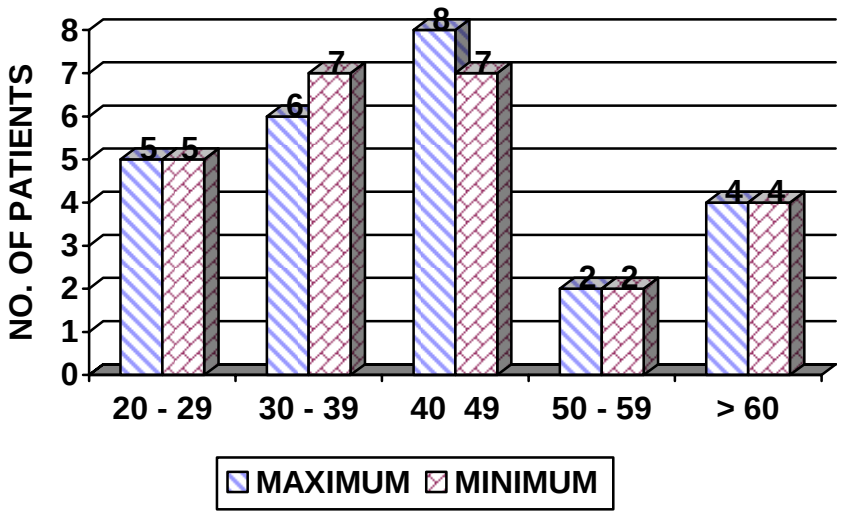


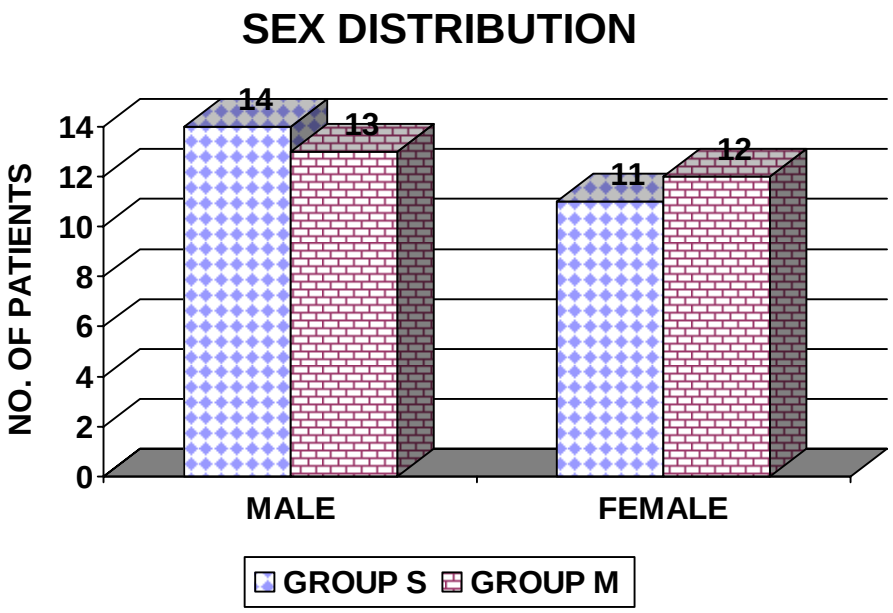
Section of lumbar vertebrae



Patient in forward flexion; Tuffier's line is shown.

AGE DISTRIBUTION




SEX DISTRIBUTION
NO. OF PATIENTS
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2
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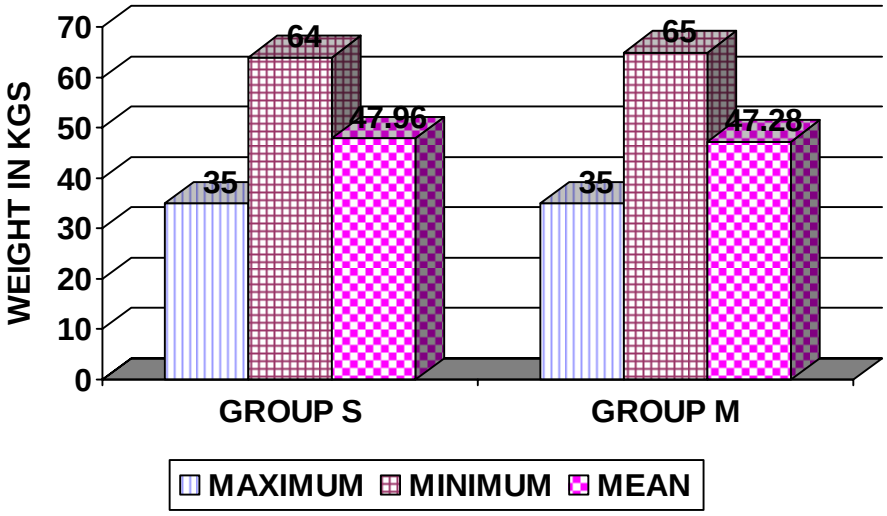
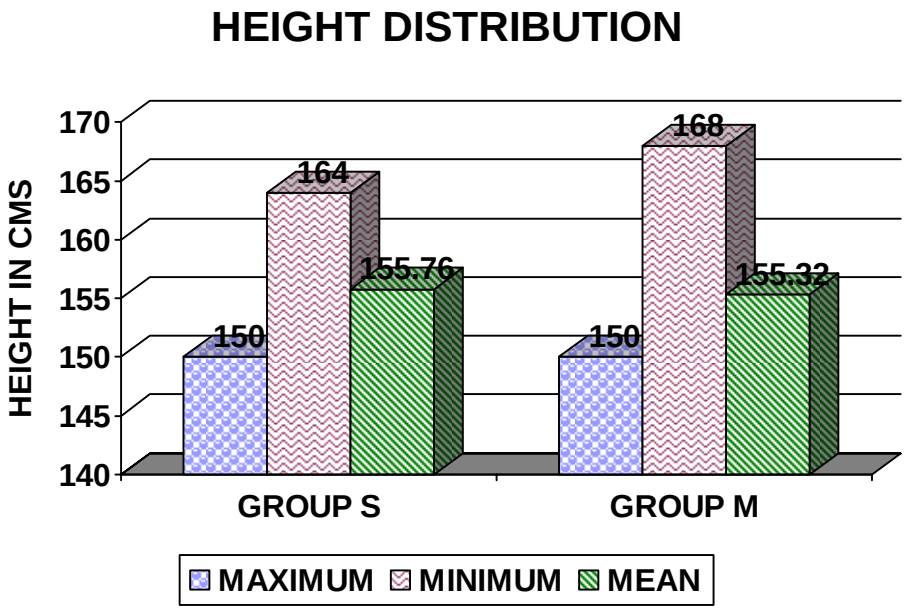
6
8
10
12
14
14
13
11
12
MALE
FEMALE
GROUP S
GROUP M

WEIGHT DISTRIBUTION




HEIGHT DISTRIBUTION
HEIGHT IN CMS
170
165
160
155
150
145
140
150
164
155.76
150
168
155.32
GROUP S
GROUP M
MAXIMUM
MINIMUM
MEAN

DURATION OF ANALGESIA